

## SCIENTIFIC LETTER

## Incidence of pericardial effusion during attacks of familial Mediterranean fever

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Familial Mediterranean fever (FMF) is an autosomal recessive disorder that affects primarily Jews, Armenians, Turks, and Arabs. It is characterised by recurrent, self limited attacks of fever accompanied by inflammation of the peritoneal, synovial, and pleural surfaces.<sup>1</sup> Pericardial involvement is a well known (0.7–1.4%) but rare feature of the disease.<sup>2,3</sup> Our initial observation of two patients who had recurrent pericarditis as a sole manifestation of FMF<sup>4</sup> has led us to suggest that pericardial inflammation is more prevalent than generally believed. Since echocardiography is a non-invasive and sensitive tool for the detection of pericardial effusion, we undertook an echocardiographic study to assess the exact frequency of pericardial effusions during attacks of FMF.

## PATIENTS AND METHODS

Two dimensional, M mode, and Doppler echocardiographic examinations were performed during 55 consecutive FMF attacks in 42 patients (15 female, 17 male). Echocardiographic study was carried out by one of the authors (ET or SA) and reviewed by the other one, who was aware of the diagnosis of FMF but unaware of the presence or absence of chest pain. Typical attacks of FMF consisted of fever and serositis including peritoneum, synovium, and pleura lasting 1–4 days. Attacks of FMF were recurrent and self limited. FMF was diagnosed according to established clinical criteria or molecular analysis when appropriate (in 37 patients).<sup>1</sup> None of the patients had amyloidosis. Patients who had evidence of congestive heart failure, uraemia, or other systemic illnesses known to be associated with pericardial disease were excluded from the study. A detailed cardiac physical examination, 12 lead ECG, and chest radiography were performed for all patients. Presence of pericardial effusion was evaluated from the posterior wall of the left ventricle at end diastole by M mode and two dimensional echocardiography with a Sonos 5500 (Hewlett Packard, Andover, Massachusetts, USA) echocardiography machine. The presence of pericardial effusion was defined as  $\geq 2$  mm echo-free space between the pericardial layers of the left ventricular posterior wall at end diastole.

Age at onset of the disease, age at diagnosis, treatment with colchicine, and the type of FMF attack during the echocardiographic study were recorded for all patients. A signed informed consent form was obtained from each parent or patient.

## RESULTS

The age of the patients ranged from 5.5–22 years (mean (SD) 10.9 (3.7) years). During the echocardiographic study 27 patients had been treated with colchicine for 6 months to 15 years (mean (SD) 45 (32.3) months), and the remaining 15 were not receiving colchicine. Chest pain was present in 24 of 55 attacks. None of the patients had other clinical findings, such as friction rub, suggesting pericarditis. All patients were

found to have normal ECG and chest radiographic studies during the attacks. Echocardiographic study showed minimal pericardial effusion during two attacks of two patients (8 and 9 year old boys). The amount of pericardial effusion was 4 mm in the first and 6 mm in the second case. Effusions resolved spontaneously on control echocardiogram at the end of the attacks. The type of clinical exacerbations in patients who had pericardial effusion was chest attack type in one and abdominal attack type in the other case. Both patients with pericardial effusion had been taking colchicine (for six months and two years). Thus, the frequency of pericardial effusion diagnosed by echocardiography during the FMF attacks was found to be 2 in 55 (3.6%). Although echocardiographic examination did not show any effusion, the presence of chest pain strongly suggested pericardial inflammation in six attacks of three other patients.

FMF mutations were found in both alleles in 27 patients and in a single allele in seven patients. No mutation was detected in three patients. M694V was the most common mutation, followed by M680I and V726A. The mutation distribution was similar to that in patients with FMF in various studies from Turkey.<sup>5,6</sup> Mutations of two patients with pericardial effusion were M694V/V726A and M694I/–. A second mutation could not be identified in the latter patient.

## DISCUSSION

Although pericarditis is regarded as one of the clinical features of FMF,<sup>4</sup> pericardial involvement has not been mentioned much in large series of FMF.<sup>7</sup> Thus, whether pericarditis is a manifestation of FMF or a coexisting, intercurrent illness has been debated. Re-evaluation of pericardial involvement in a recent study showed a 0.7% prevalence of pericarditis in 1553 thoracic attacks of 3976 patients with FMF. This study clearly showed that pericarditis was a manifestation of FMF.<sup>2</sup> Similarly, the prevalence of definite pericardial attacks has recently been reported as 1.4% (34 of 2468 patients) by the Turkish FMF Study Group.<sup>3</sup> Both studies show that pericarditis is a rare manifestation of FMF as compared with the other forms of serositis.

Why pericardium is not involved as commonly as other serosal membranes is unknown. It has been suggested that underdiagnosis may partly be responsible for the infrequent detection of pericarditis. If echocardiography were used to detect pericarditis in every attack of FMF (especially for chest attacks), it would be possible to detect pericardial attacks more frequently. Our present study, however, shows that pericardial effusion is not a frequent manifestation of FMF, even with the use of echocardiography. Only one prospective echocardiographic study was undertaken before ours, by Dabestani and colleagues.<sup>8</sup> They reported a much higher (27%) prevalence of pericardial involvement in predominantly adult patients with FMF. However, Dabestani and colleagues described pericardial disease as an effusion in the

pericardial space or pericardial thickening detected only by M mode echocardiography. It is known that if two dimensional and M mode echocardiography are used together, diagnostic acuity of echocardiography to detect pericardial effusion is increased. Since it is difficult to detect a thickened pericardium with echocardiography, the reliability of echocardiographic diagnosis is questionable. Thus, the high prevalence of pericardial disease that Dabestani and colleagues found in their echocardiographic study may have been an overestimation caused by the method used to define pericardial disease.

Another possible explanation of this discrepancy is the difference in the ages of the patients. Since pericarditis tends to appear at a late stage of FMF, a higher prevalence may be predicted in adult patients than in children.<sup>2</sup> It is known that colchicine is effective for the treatment of recurrent, refractory pericardial effusions resulting from miscellaneous causes other than FMF.<sup>9</sup> Although colchicine may prevent the occurrence of pericardial fluid in patients with these disorders, no study to date has reported that colchicine can blunt any type of FMF attacks. Moreover, both of our patients with pericardial effusion had been taking colchicine.

Previous clinical studies and the results of our study show that pericardial attacks are infrequent manifestations of FMF, and routine echocardiographic screening is not necessary in FMF attacks.

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### Job strain and high work demands and lack of opportunity to control work are related to increased risk of coronary heart disease in British government employees

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**T**he Whitehall II study has followed prospectively over 10 000 London based civil servants (government department employees) for a mean of 11 years, in particular identifying those who developed coronary heart disease (CHD). Data were collected on known coronary risk factors and self-reported questionnaires detailed such work characteristics as job demands and decision latitude (degree of control over skill use, time allocation and authority to make decisions).

Those with high scores in both areas were defined as having “job strain”. They proved to be at the greatest risk of CHD, regardless of their coronary risk factors or domestic psychosocial support (hazard ratio 1.57 (CI 1.26–1.96)). A high score for either of the components also led to a higher risk of CHD.

The authors suggest the policy implications of their research are that strategies for work place health promotion should rely on redesigning jobs by reducing psychological demands and increasing individuals’ say in decisions about their work as well as offering more variety in job tasks. The next step should be intervention studies to evaluate the utility of any such changes.

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